

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Diagnostics Assessment Programme

### High-sensitivity troponin for the early rule out of acute myocardial infarction

#### Final scope – guidance update

September 2019

#### **1 Introduction**

Since the publication of NICE diagnostics guidance on [early rule out of acute myocardial infarction using high-sensitivity troponin tests](#) (DG15) in October 2014, the recommended technologies in the guidance have been selected as a 'rapid uptake product' by the [Accelerated Access Collaborative \(AAC\)](#). To support the work of the AAC in implementing these technologies, the guidance review decision (published in April 2018) has been considered and NICE has decided that the Diagnostics Assessment Programme will update this guidance.

The NICE guideline on [chest pain of recent onset: assessment and diagnosis \(CG95\)](#) will no longer review the evidence on high-sensitivity troponin tests, as stated in the guidance review decision, but, instead, will align to the diagnostics guidance once the update is published. As the update of this guidance was initiated by the Accelerated Access Collaborative (AAC) aspects of the process will vary from the published process of the Diagnostics Assessment Programme to allow the guidance to be updated as efficiently as possible.

The following questions have been highlighted by stakeholders and the accelerated access collaborative as priorities to be answered in this update.

- Is there sufficient evidence to recommend the use of specific early rule-out testing protocols within 1 hour and within 3 hours?
- Can the limit of detection of an assay be used as a threshold in an early rule-out testing protocol?
- Are there new high-sensitivity troponin tests that should be included in the guidance?
- Should sex-specific cut-offs be used?

A glossary of terms is provided in appendix A.

## **2 Description of the technologies**

This section describes the properties of the diagnostic technologies based on information provided to NICE from the companies and on information available in the public domain. NICE has not carried out an independent evaluation of these descriptions.

### **2.1 Purpose of the medical technologies**

Cardiac troponin I and cardiac troponin T are biological markers of cardiac muscle death (cardiomyocyte necrosis). They are released into the circulation when damage to cardiac muscle has occurred. A rise or fall in troponin levels can signify that myocardial damage has occurred. The optimum sensitivity of older (non-high-sensitivity) troponin assays (hereafter referred to as standard troponin assays) for acute MI occurs 10–12 hours after the onset of symptoms. For many people, this results in the need for hospital admission and observation while serial troponin testing is carried out. To overcome this, high-sensitivity troponin assays have been developed. These are able to detect lower levels of troponin in the blood earlier than older standard assays, leading to improved early detection of acute MI.

Using these high-sensitivity assays enables earlier detection of changes in troponin levels. This allows non-ST-segment elevation myocardial infarction (NSTEMI) to be ruled out within 4 hours, if test results are available within 3 hours of presentation to the emergency department or chest pain units. The increased sensitivity of these assays could mean a shorter inpatient hospital stay for people without raised levels of troponin and earlier intervention for those with a confirmed NSTEMI. As with older standard troponin assays, the high-sensitivity assays are intended to be used with clinical history taking and the electrocardiogram to diagnose NSTEMI because, despite being highly specific for cardiomyocyte necrosis, troponin may also be raised in people who do not have underlying evidence of ischaemic heart disease. Conditions other than acute MI that may cause troponin levels to be raised include myocarditis, congestive heart failure, severe infections, musculoskeletal conditions and renal disease.

### **2.2 Product properties**

High-sensitivity troponin tests are indicated for use in people presenting to an emergency department with acute chest pain, and who do not have evidence of ST-elevation on a resting 12-lead ECG, that is people with a suspected non-ST-segment-elevation acute coronary syndrome (NSTEMI-ACS). NSTEMI-ACS includes both NSTEMI and unstable angina, conditions which require different treatment strategies (Hamm et al, 2011).

International guidelines recommend that in order to be classified as high-sensitivity, troponin assays should have a coefficient of variation (CV) of 10% or less at the 99th percentile upper limit of the reference population and should be able to detect troponin in at least 50% of the reference population at a concentration value that is above the assay's limit of detection (Apple et al. 2017). In the context of NSTEMI-ACS the term "reference population" refers to a healthy population who would not be expected to have elevated troponin levels. A range of high-sensitivity troponin I and troponin T assays are currently available for use in a clinical laboratory setting; Table 1 (below) summarises the product properties of the high-sensitivity troponin assays that are available to the NHS. Since the publication of DG15, the AccuTnl+3 assay (Beckman Coulter) has been withdrawn from the UK. The tests listed below are those that were included in DG15, or from companies who have registered as stakeholders for this update and provided information on their products.

## **Troponin T assays**

### *2.2.1 The Elecsys troponin T high-sensitive assay (Roche)*

The Elecsys troponin T high-sensitive assay and the Elecsys troponin T high-sensitive STAT assay are designed for use in a laboratory setting. The Elecsys troponin T high-sensitive assay (200 test pack) and Elecsys troponin T high-sensitive STAT assay (100 test pack) can be used on the Roche cobas e411, e 601, and e602 analysers. The company state that the performance characteristics are equivalent when used on these analysers. The assay can also be run on the cobas e801 analyser which is designed for very high throughput as both a standard and STAT assay. This requires the test to be purchased as a 300 test pack, the reagents are the same as the 100 and 200 test packs but the application on the cobas e801 analyser results in a lower limit of detection (see table 1) The Elecsys test is a sandwich electrochemiluminescence immunoassay, and is intended for the in-vitro quantitative determination of troponin T in serum and plasma samples. Results are available within 18 minutes with the standard assay and within 9 minutes if the STAT assay is used. The Elecsys assays can detect troponin T in 57% of the reference population and have a recommended 99<sup>th</sup> percentile cut-off of 14 ng/L with a CV of less than 10%. Sex specific 99th percentile cut offs of 9 ng/L for females and 16.8 ng/L for males are also provided. The assays are CE marked and available to the NHS.

## **Troponin I assays**

### *2.2.2 Access hsTnl assay (Beckman Coulter)*

The Access hsTnI is designed for use in a laboratory setting with the Beckman Coulter Access 2 and Dxl/DxC analysers. It is a paramagnetic particle chemiluminescent immunoassay, and is intended for the in-vitro quantitative determination of troponin I in serum and plasma samples. The turnaround time of the assay is 17 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 17.5 ng/L for the whole population, 11.6 ng/L for females and 19.8 ng/L for males. Each 99<sup>th</sup> percentile has a CV of less than 10%. The assay can detect troponin I in >97% of the reference population. The assay is CE marked and available to the NHS. The company states that the performance of the assay does not differ by analyser.

### *2.2.3 ARCHITECT high-sensitivity troponin I assay (Abbott Diagnostics)*

The ARCHITECT high-sensitivity troponin I STAT assay is designed for use in a laboratory setting and can be used with the Abbott ARCHITECT i2000SR and i1000SR analysers. The assay is a chemiluminescent microparticle immunoassay and is intended for the in-vitro quantitative determination of troponin I in serum and plasma samples. Results are available within 18 minutes. The ARCHITECT high-sensitivity troponin I STAT assay can detect troponin I in 96% of the reference population, and has a recommended 99<sup>th</sup> percentile cut-off of 26.2ng/L with a CV of 4%. Sex specific 99<sup>th</sup> percentile cut offs of 15.6 ng/L for females (CV of 5.3%) and 34.2 ng/L for males (CV of 3.5%) are also provided. The assay is CE marked and available to the NHS.

### *2.2.4 Alinity i STAT High Sensitive Troponin-I assay (Abbott Diagnostics)*

The Alinity i STAT High Sensitive Troponin-I assay is designed for use in a laboratory setting and can be used with the Alinity i analyser. It is a chemiluminescent microparticle immunoassay used for the quantitative determination of troponin I in plasma and serum samples. Results are available within 18 minutes. The Alinity i STAT High Sensitive Troponin-I assay has a recommended 99<sup>th</sup> percentile cut-off of 26.2 ng/L with a CV of 4.6%. Sex specific 99<sup>th</sup> percentile cut offs of 15.6 ng/L for females (CV of 5.0%) and 34.2 ng/L for males (CV of 4.5%) are also provided. The assay is CE marked and available to the NHS.

### *2.2.5 ADVIA Centaur high-sensitivity troponin I assay (Siemens Healthineers)*

The ADVIA Centaur high-sensitivity troponin I assay is designed for use in a laboratory setting with the Siemens ADVIA Centaur XP and ADVIA Centaur XPT analysers. It is a magnetic latex particle chemiluminescent immunoassay, and is intended for the in-vitro quantitative determination of troponin I in serum and plasma samples. Test results are available in 18 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 47.34 ng/L for the whole population in lithium heparin and of 46.47 ng/l in serum. Sex specific

99th percentile cut offs of 36.99 ng/L for females and 57.27 ng/L for males in lithium heparin and 39.59 ng/L for females and 58.05 ng/L for males in serum are also provided. Each 99<sup>th</sup> percentile has a CV of less than 10%. The assay can detect troponin I in more than 50% of the reference population. The assay is CE marked and available to the NHS.

#### *2.2.6 Atellica IM High-sensitivity troponin I assay (Siemens Healthineers)*

The Atellica IM high-sensitivity troponin I assay is designed for use in a laboratory setting with the Siemens Atellica IM analyser. It is a magnetic latex particle chemiluminescent immunoassay, and is intended for the in-vitro quantitative determination of troponin I in serum and plasma samples. Test results are available in 10 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 45.2 ng/L for lithium heparin and 45.43 ng/L for serum. Sex specific 99<sup>th</sup> percentile cut offs of 34.11 ng/L for females and 53.48 ng/L for males in lithium heparin and 38.64 ng/L for females and 53.53 ng/L for males in serum are provided. Each 99<sup>th</sup> percentile has a CV of less than 10%. The assay can detect troponin I in more than 50% of the reference population. The assay is CE marked and available to the NHS.

#### *2.2.7 Dimension EXL High-sensitivity troponin I assay (Siemens Healthineers)*

The Dimension EXL high-sensitivity troponin I assay is designed for use in a laboratory setting with the Siemens Dimension EXL analyser. It is a magnetic latex particle chemiluminescent immunoassay, and is intended for the in-vitro quantitative determination of troponin I in serum and plasma samples. Test results are available in 18 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 60.4 ng/L for lithium heparin and 58.2 ng/L for serum. Sex-specific 99<sup>th</sup> percentile cut offs of 51.4 ng/L for females and 76.2 ng/L for males in lithium heparin and 47.8 ng/L for females and 71.8 ng/L for males in serum are provided. Each 99<sup>th</sup> percentile has a CV of less than 10%. The assay can detect troponin I in more than 50% of the reference population. The assay is CE marked and available to the NHS.

#### *2.2.8 Dimension Vista high-sensitivity troponin I assay (Siemens Healthineers)*

The Dimension Vista high-sensitivity troponin I assay is designed for use in a laboratory setting with the Siemens Dimension Vista analysers. It is a magnetic latex particle chemiluminescent immunoassay, and is intended for the in-vitro quantitative determination of troponin I in serum and plasma samples. Test results are available in 10 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 58.9 ng/L for lithium heparin and 57.9% for serum. Sex specific 99<sup>th</sup> percentile cut offs of 53.77 ng/L for females and 78.5 ng/L for males in lithium heparin and 51.1 ng/L for females and 74.9 ng/L for males in

serum are provided. Each 99<sup>th</sup> percentile has a CV of less than 10%. The assay can detect troponin I in more than 50% of the reference population. The assay is CE marked and available to the NHS.

#### *2.2.9 TriageTrue High Sensitivity Troponin I Test (Quidel Cardiovascular)*

The TriageTrue High Sensitivity Troponin I test can be used in a near patient setting or in a laboratory with the Triage MeterPro analyser. It is a fluorescence immunoassay and is intended for the in-vitro quantitative determination of troponin I in EDTA anticoagulated whole blood and plasma samples. Test results are available in less than 20 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 20.5 ng/L with a CV of less than 10%. Sex specific 99<sup>th</sup> percentile cut offs of 14.4 ng/L for females and 25.7 ng/L for males are provided. The test can detect troponin I in more than 50% of the reference population. The test is CE marked and available to the NHS.

#### *2.2.10 VITROS High Sensitivity Troponin I Assay (Ortho Clinical Diagnostics)*

The VITROS High Sensitivity Troponin I assay is designed for use in a laboratory setting on the following analysers: VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated System. It is an immunometric immunoassay and is intended for the in-vitro quantitative determination of troponin I in serum and plasma samples. Test results are available in 15 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 11 ng/L for both lithium heparin and serum samples. Sex specific 99<sup>th</sup> percentile cut offs of 9 ng/L (in lithium heparin and serum) for females and 13 ng/L (in lithium heparin) and 12 ng/L (in serum) for males are provided. The assay can detect troponin I in more than 50% of the reference population. The assay is CE marked and available to the NHS.

#### *2.2.11 VIDAS High sensitive Troponin I assay (Biomérieux)*

The VIDAS High sensitive Troponin I assay is designed for use in a laboratory setting on the following analysers: VIDAS, MINI VIDAS and VIDAS 3. It is intended for the in-vitro quantitative determination of troponin I in serum and plasma (lithium heparin) samples. Test results are available in 20 minutes. It has a recommended 99<sup>th</sup> percentile cut-off of 19 ng/L. Sex specific 99<sup>th</sup> percentile cut offs of 11 ng/L for females and 25 ng/L for males are provided. The assay is CE marked and available to the NHS.

**Table 1 – Summary of key high-sensitivity troponin I and troponin T assay characteristics**

Manufacturer	System and compatible analysers	Assay	99 <sup>th</sup> percentile (ng/L)	CV at 99 <sup>th</sup> percentile	% of reference population cTn detected in	Turn-around time	LoD	LOQ
Abbott Diagnostics	ARCHITECT i1000sr and i2000sr	ARCHITECT HsTnI	Overall: 26.2 ng/L Female: 15.6 ng/L Male: 34.2 ng/L	Overall: 4.0% Female: 5.3% Male: 3.5%	96% (Apple et al. 2012)	18 minutes	1.9 ng/L	4.7 ng/L (10% CV); 1.3 ng/L (20% CV)
Abbott Diagnostics	Alinity i	Alinity hsTnI	Overall: 26.2 ng/L Female: 15.6 ng/L Male: 34.2 ng/L	Overall: 4.6% Female: 5.0% Male: 4.5%	96% (Apple et al. 2012)	18 minutes	1.6 ng/L	3.7 ng/L (10% CV); 2.1 ng/L (20% CV)
Beckman Coulter <sup>1</sup>	Access 2, Dxl 600/800, DxC 600i/880i /860i/680i/660i	Access hsTnI	Overall: 17.5 ng/L Female: 11.6 ng/L Male: 19.8 ng/L	Overall: 3.7% Female: 4.2% Male: 3.6%	97.1% to >99%	17 minutes	2.3 ng/L	2.3ng/L
Roche <sup>1</sup>	200 test pack: cobas e411, e601, e602 300 test pack cobas: e801	Elecsys TnT-hs	Overall: 14 ng/L Female: 9 ng/L Male: 16.8 ng/L	<10%	57%	18 minutes	5 ng/L (3ng/L on Cobas e801)	13 ng/L
Roche <sup>1</sup>	100 test pack: cobas e411, e601, e602, 300 test pack: cobas e801	Elecsys TnT-hs STAT	Overall: 14 ng/L Female: 9 ng/L Male: 16.8 ng/L	<10%	57%	9 minutes	5ng/L (3ng/L on Cobas e801)	13 ng/L
Siemens Healthineers <sup>1</sup>	Atellica	Atellica IM High-sensitivity troponin I	Lithium heparin: Overall: 45.2 ng/L Female: 34.11 ng/L Male: 53.48 ng/L	<4%	75%	10 minutes to first result	1.6 ng/L	2.5 ng/L

Manufacturer	System and compatible analysers	Assay	99 <sup>th</sup> percentile (ng/L)	CV at 99 <sup>th</sup> percentile	% of reference population cTn detected in	Turn-around time	LoD	LOQ
			Serum: Overall: 45.43 ng/L Female: 38.64 ng/L Male: 53.53 ng/L					
Siemens Healthineers <sup>1</sup>	Dimension EXL	Dimension EXL High-sensitivity troponin I	Lithium heparin: Overall: 60.4 ng/L Female: 51.4 ng/L Male: 76.2 ng/L	<5%	>50%	10 minutes to first result	2.7 ng/L	4.0 ng/L
			Serum: Overall: 58.2 ng/L Female: 47.8 ng/L Male: 71.8 ng/L					
Siemens Healthineers <sup>1</sup>	Dimension Vista	Dimension Vista high-sensitivity troponin I	Lithium heparin: Overall: 58.9 ng/L Female: 53.7 ng/L Male: 78.5 ng/L	<5%	>50%	10 minutes to first result	2.0 ng/L	3.0 ng/L
			Serum: Overall: 57.9 ng/L Female: 51.1 ng/L Male: 74.9 ng/L					
Siemens Healthineers <sup>1</sup>	ADVIA Centaur XP and ADVIA Centaur XPT	ADVIA Centaur high-sensitivity	Lithium heparin: Overall: 47.34 ng/L Female: 36.99 ng/L	<4.9%	63%	18 minutes to first result	1.6 ng/L	2.5 ng/L



Manufacturer	System and compatible analysers	Assay	99 <sup>th</sup> percentile (ng/L)	CV at 99 <sup>th</sup> percentile	% of reference population cTn detected in	Turn-around time	LoD	LOQ
		troponin I	Male: 57.27 ng/L					
			Serum: Overall: 46.47 ng/L Female: 39.59 ng/L Male: 58.05 ng/L					
Quidel Cardiovascular	Triage MeterPro	TriageTrue High Sensitivity Troponin I Test	Overall: 20.5 ng/L Female: 14.4 ng/L Male: 25.7 ng/L	<10%	>50%	<20 minutes	Plasma: 0.7-1.6 (ng/L) Blood: 1.5-1.9 (ng/L)	Plasma: 2.1-3.6 (ng/L) Blood: 2.8-2.8 (ng/L)
Ortho Clinical Diagnostics	VITROS ECI/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems	VITROS High Sensitivity Troponin I	Overall: 11 ng/L Female: 9 ng/L Male: 13 ng/L (lithium heparin) Male: 12 ng/L (serum)	≤10%	≥50%	15 minutes to first result	ECi/ECiQ: 0.86 ng/L 3600: 0.39 ng/L 5600: 0.43 ng/L XT7600: 0.42 ng/L	1.23 ng/L
Biomérieux	VIDAS, MINI VIDAS AND VIDAS 3	VIDAS High sensitive Troponin I	Overall: 19 ng/L Female: 11 ng/L Male: 25 ng/L	7.0%	TBC	20 minutes	1.3-3.2 ng/L	2.9-4.9 ng/L

<sup>1</sup> Information provided by company to NICE.  
Abbreviations: cTn cardiac troponin, LoD limit of detection, LoQ limit of quantitation, TBC to be confirmed

### 3 Clinical need and practice

Background on the condition and the diagnostic and care pathways are described in [DG15](#). Since publication of DG15, NICE’s clinical guideline on [chest pain of recent onset](#) has been updated to include high sensitivity troponin tests. However, stakeholder feedback from the accelerated access collaborative suggests that high sensitivity troponin testing used with early rule out protocols has not been routinely adopted in the NHS, and where it has been adopted there is wide variation in how the tests and protocols have been implemented. Therefore, the comparator for this assessment will remain standard troponin testing over 10–12 hours from symptom onset to capture the benefit of high sensitivity troponin assays used in combination with early rule-out protocols.

### 4 Scope of the assessment

**Table 2: Scope of the assessment**

<b>Decision question</b>	Does early rule out of acute myocardial infarction using high-sensitivity troponin testing within 4 hours of presentation (including 1 hour and 3 hour rule out) represent a more cost-effective use of NHS resources compared to serial troponin measurement over 10-12 hours?
<b>Populations</b>	<p>People with chest pain and a suspected non-ST-segment-elevation acute coronary syndrome.</p> <p>Subgroups for consideration include groups where different cut-off levels for determining a positive troponin test may be required. Subgroups may include:</p> <ul style="list-style-type: none"><li>• Sex</li><li>• People who may have chronically elevated troponin levels for example older people and people with renal disease</li></ul> <p>The analysis should also consider subgroups with low and high pre-test probabilities for NSTEMI, for example people with a history of previous AMI, and time since symptom onset.</p>
<b>Interventions</b>	<p>High-sensitivity troponin tests, used either as a single test or series of tests, within 4 hours of presentation (including 1 hour and 3 hour rule out). High-sensitivity troponin assays identified as of interest to the NHS are:</p> <ul style="list-style-type: none"><li>• Access hsTnI (Beckman Coulter)</li><li>• ADVIA Centaur high-sensitivity troponin I (Siemens Healthineers)</li></ul>

	<ul style="list-style-type: none"> <li>Alinity i STAT High Sensitive Troponin-I assay (Abbott Diagnostics)</li> <li>ARCHITECT STAThs-cTnI (Abbott Diagnostics)</li> <li>Atellica IM high-sensitivity troponin I (Siemens Healthineers)</li> <li>Dimension EXL high-sensitivity troponin I (Siemens Healthineers)</li> <li>Dimension Vista high-sensitivity troponin I (Siemens Healthineers)</li> <li>Elecsys cTnT-hs (Roche Diagnostics)</li> <li>Elecsys cTnT-hs STAT (Roche Diagnostics)</li> <li>TriageTrue High Sensitivity Troponin I Test (Quidel Cardiovascular)</li> <li>VIDAS High sensitive Troponin I assay (Biomérieux)</li> <li>VITROS High Sensitivity Troponin I Assay (Ortho Clinical Diagnostics)</li> </ul>
<b>Comparator</b>	<ul style="list-style-type: none"> <li>Serial cardiac troponin testing with a 10-12 hour peak measurement test strategy. Comparator technologies may include any troponin assay not previously defined as an intervention.</li> </ul>
<b>Healthcare setting</b>	Emergency Department
<b>Outcomes</b>	<p>Intermediate measures for consideration may include:</p> <ul style="list-style-type: none"> <li>Diagnostic accuracy including at 99<sup>th</sup> percentile cut-off levels, limit of detection and limit of quantitation, and considering delta change</li> <li>Turnaround time</li> <li>Time to discharge</li> <li>Proportion of people admitted and discharged</li> <li>Proportion of people diagnosed with NSTEMI</li> </ul> <p>Clinical outcomes for consideration may include:</p> <ul style="list-style-type: none"> <li>Subsequent emergency department attendance or hospital admission for chest pain</li> <li>Patient anxiety associated with waiting for a clinical decision and the initiation of further treatment</li> <li>Morbidity and mortality, including fatal and non-fatal acute myocardial infarction after discharge from the emergency department</li> <li>Frequency of coronary revascularisation</li> <li>Prognostic accuracy for major adverse cardiac events, that is death, non-fatal MI,</li> </ul>

	<p>revascularisation, or hospitalisation for myocardial ischaemia.</p> <ul style="list-style-type: none"> <li>• Health related quality of life</li> </ul>
	<p>Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:</p> <ul style="list-style-type: none"> <li>• Costs for high-sensitivity troponin testing including early rule out test strategies at various time points within 4 hours of presentation</li> <li>• Costs associated with a diagnosis of NSTEMI including additional tests such as ECG, hospital admission, treatment and follow-up</li> <li>• Cost of adverse events arising as a result of testing including subsequent emergency department attendances or re-admissions.</li> </ul>
	<p>The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.</p>
<b>Time horizon</b>	<p>The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p>

## 5 Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Consideration should be given to the use of sex-specific cut-offs which are recommended by the companies for some products. Troponin levels may be chronically elevated in some groups; this includes people who are older and people with comorbidities such as chronic kidney disease. Consideration may need to be given to these groups when exploring cut-offs and early rule-out protocols which include delta change to define a positive or negative result.

## 6 Implementation issues

The NICE adoption team has identified potential barriers to the implementation of high sensitivity troponin:

- Access to a recommended high-sensitivity troponin assay.
- Agreement between emergency department, cardiology, clinical biochemistry and acute medicine about the most appropriate early rule-out protocol.
- Inappropriate testing reducing clinical confidence in the test.

- Allocation of resources: anticipated savings will be seen in emergency department, cardiology and acute medicine through quicker discharge; costs are likely to be incurred by the laboratory (assay, consumables and staff costs).

Any laboratories using high-sensitivity assays should be able to show compliance with an accredited external quality assurance scheme. Internal quality assurance and calibration of all tests should also be conducted in accordance with the manufacturer's instructions for use.

## Appendix A Glossary of terms

**Acute coronary syndrome (ACS):** an umbrella term for a range of conditions where myocardial ischaemia may be present. ACS includes STEMI, NSTEMI and unstable angina. Suspected ACS presents a challenge for clinicians who must use a range of diagnostic tests to determine the underlying condition and instigate the correct management.

**Coefficient of variation (CV):** Intra-assay coefficient of variation is used to describe the precision, or repeatability, of immunoassays. In order to be classified as high-sensitivity, troponin assays are required to demonstrate a CV of less than 10%.

**Delta change:** A measure of the magnitude of change between baseline and serial test values.

**Limit of detection:** The lowest level of an analyte that can be reliably detected or distinguished from the absence of the analyte.

**Limit of quantitation:** The lowest level of an analyte that can be reliably detected and for which predefined targets for bias and imprecision can be met.

**Non-ST-elevation acute coronary syndrome:** A working diagnosis given to patients who present with a suspected acute coronary syndrome, without persistent ST-elevation changes on a 12-lead ECG.

**Non-ST-elevation myocardial infarction (NSTEMI):** A less severe myocardial infarction which occurs when the coronary artery is partially blocked, meaning that less damage to the myocardium occurs than would be observed with a STEMI. NSTEMI does not produce ST elevation on ECG and the use of cardiac biomarkers is required to distinguish a NSTEMI from unstable angina. NSTEMI is distinguished from unstable angina on the basis of raised cardiac biomarkers, usually troponin.

**STAT (Short Turn Around Time) test:** Tests that are required to be processed quickly to facilitate the management of an emergency. Tests marked as “STAT” are treated as the highest priority for processing and reporting by a laboratory.

**ST-elevation myocardial infarction (STEMI):** A more severe myocardial infarction which is diagnosed by observing a characteristic elevation of the ST segment on an ECG. An elevation of the ST segment indicates that a relatively large amount of damage to the myocardium has occurred, usually because the coronary artery is blocked.

## **Appendix B      References**

Apple FS, Ler R and Murakami MM (2012) Determination of 19 cardiac troponin I and T assay 99th percentile values from a common presumably healthy population. *Clin Chem*; 58(11): 1574-81

Apple FS, Sandoval Y, Jaffe AS and Ordonez-Llanos J (2017) Cardiac troponin assays: Guide to understanding analytical characteristics and their impact on clinical care. *Clin Chem*; 63 (1): 73-81.

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